

4,700,000 Shares of Common Stock Pre-Funded Warrants to Purchase up to 6,750,382 Shares of Common Stock Up to 6,750,382 Shares of Common Stock Underlying the Pre-Funded Warrants

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering in a registered direct offering to an accredited investor, 4,700,000 shares (the "Shares") of our common stock and pre-funded warrants to purchase up to 6,750,382 shares of our common stock (the "Pre-Funded Warrants"). The offering price per Share and per Pre-Funded Warrant is \$0.655 and \$0.654, respectively. The Pre-Funded Warrants will have an exercise price of \$0.001 per share and will be exercisable upon issuance until exercised in full.

In a concurrent private placement, we are also issuing to the purchaser of the Shares and the Pre-Funded Warrants, warrants to purchase up to 11,450,382 shares of our common stock (the "Purchase Warrants"). Each Purchase Warrant will be exercise price of \$0.53 per share. The Purchase Warrants and the shares of common stock issuable upon the exercise of such warrants are not being registered under the Securities Act of 1933, as amended (the "Securities Act"), are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided in Securities Act.

Our common stock and warrants outstanding prior to this offering are listed on the Nasdaq Capital Market under the symbols "EFTR" and "EFTRW," respectively. On May 25, 2023, the closing price of our common stock was \$0.529 per share and the closing price of our warrants was \$0.13 per warrant. However, there is no established public trading market for the Pre-Funded Warrants, and we do not expect a market to develop. In addition, we do not intend to list the Pre-Funded Warrants on the Nasdaq Capital Market, any other national securities exchange or any other nationally recognized trading system.

As of May 24, 2023, the aggregate market value of our outstanding common stock held by non-affiliates ("public float") was approximately \$26.5 million, based on 34,656,628 shares of outstanding common stock held by non-affiliates as of such date, and a price of \$0.7656 per share, which was the last reported sales price of our common stock on the Nasdaq Capital Market on May 22, 2023. We have not offered or sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the prior 12-calendar-month period that ends on and includes the date of this prospectus supplement other than approximately \$0.5 million of shares of common stock sold under the Controlled Equity OfferingSM Sales Agreement, dated September 1, 2022, with Cantor Fitzgerald & Co. during the last 12 calendar months. Accordingly, based on the foregoing, we are currently eligible under General Instruction I.B.6 of Form S-3 to offer and sell shares of our common stock having an aggregate offering price of up to approximately \$8.3 million. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and a smaller reporting company as defined under Rule 405 of the Securities Act, and, as such, are subject to certain reduced public company reporting requirements.

An investment in our securities involves a high degree of risk. Please read "<u>Risk Factors</u>" on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before investing in our securities.

We have engaged H.C. Wainwright & Co., LLC (the "placement agent"), as our exclusive placement agent in connection with this offering. The placement agent has no obligation to buy any of the securities from us or to arrange for the purchase or sale of any specific number or dollar amount of the securities. We have agreed to pay the placement agent the fees set forth in the table below. See "Plan of Distribution" in this prospectus supplement for more information regarding these arrangements.

		Per Pre-	
		Funded	
	Per Share	Warrant	Total
Offering price	\$ 0.655	\$ 0.654	\$ 7,493,249.83
Placement agent fees ⁽¹⁾	\$ 0.04585	\$ 0.04585	\$ 525,000.01
Proceeds, before expenses, to us ⁽²⁾	\$ 0.60915	\$ 0.60815	\$ 6,968,249.82

(1) We have also agreed to (i) grant warrants to purchase 801,527 shares of common stock to the placement agent, or its designees and (ii) pay the placement agent for certain expenses. See "Plan of Distribution" for additional information with respect to the compensation we will pay the placement agent.

(2) The amount of the offering proceeds to us presented in this table does not give effect to any exercise of the Pre-Funded Warrants being issued in this offering.

Delivery of our shares of common stock and Pre-Funded Warrants is expected to be made on or about May 31, 2023, subject to satisfaction of customary closing conditions.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

H.C. Wainwright & Co.

The date of this prospectus supplement is May 26, 2023.

TABLE OF CONTENTS

	Page
Prospectus Supplement	
About this Prospectus Supplement	S-1
Cautionary Note Regarding Forward-Looking Statements	S-2
Prospectus Supplement Summary	S-3
Risk Factors	S-7
Use of Proceeds	S-9
Description of Securities Offered	S-10
Private Placement Transaction	S-12
Dilution	S-14
<u>Plan of Distribution</u>	S-15
Legal Matters	S-17
Experts	S-17
Where You Can Find More Information; Information Incorporated by Reference	S-17

Prospectus

About This Prospectus	1
Where You Can Find More Information; Incorporated by Reference	2
The Company	2
	4
Risk Factors	5
Cautionary Note Regarding Forward-Looking Statements	5
<u>Use of Proceeds</u>	6
Dividend Policy	6
Description of Capital Stock	7
Description of Debt Securities	14
Description of Warrants	22
Description of Units	24
<u>Global Securities</u>	25
Plan of Distribution	29
Legal Matters	31
Experts	31

About this Prospectus Supplement

This prospectus supplement and the accompanying prospectus dated September 9, 2022 are part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission ("SEC") utilizing a "shelf" registration process. This prospectus supplement and the accompanying prospectus relate to the offer by us of shares of our common stock and Pre-Funded Warrants. We provide information to you about this offering in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus or any document incorporated by reference herein prior to the date of this prospectus supplement, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement or the accompanying prospectus we have referred you to under the heading "Where You Can Find More Information; Information Incorporated by Reference." These documents contain important information that you should consider when making your investment decision.

You should rely only on information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the placement agent has not, authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock and Pre-Funded Warrants only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our securities.

In this prospectus supplement, unless the context otherwise indicates, the terms "eFFECTOR," the "Company," "we," "our" and "us" or similar terms refer to eFFECTOR Therapeutics, Inc., including its consolidated subsidiary.

We use our trademarks in this prospectus supplement as well as trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement appear without the $^{(R)}$ and TM symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

Cautionary Note Regarding Forward-Looking Statements

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein, including statements regarding our future results of operations or financial condition, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, the timing and likelihood of regulatory filings and approvals for our product candidates, our ability to commercialize our product candidates, if approved, the impact of COVID-19 and related supply chain disruption on our business, pricing and reimbursement of our product candidates, if approved, the potential to develop future product candidates, the potential benefits of strategic collaborations, the timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "would," "could," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus supplement, and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading "Risk Factors" and elsewhere in this prospectus supplement. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigat

Prospectus Supplement Summary

This summary provides an overview of selected information contained elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all the information you should consider before investing in our securities. Therefore, you should read the entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the "Risk Factors" section, and other documents or information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making any investment decision.

Company Overview

We are a clinical-stage biopharmaceutical company focused on pioneering the development of a new class of oncology drugs we refer to as STRIs. Translation is the process in cells whereby the synthesis of proteins is directed by information contained in genetic sequences. We utilized our proprietary selective translation regulation technology platform to internally discover a portfolio of small molecule STRI product candidates. Our product candidates target the eIF4F complex and its activating kinase, mitogen-activated protein kinase interacting kinase ("MNK"). The eIF4F complex is a central node where two of the most frequently mutated signaling pathways in cancer, the PI3K-AKT and RAS-MEK pathways, converge to activate the translation of select mRNA into proteins that are frequent culprits in key disease-driving processes. Inhibition of any one of these targets simultaneously downregulates multiple disease-driving proteins before they are synthesized. Each of our product candidates is designed to act on a single protein that drives the expression of a network of multiple functionally related proteins, including oncoproteins, which are proteins whose aberrant function can cause cancer, immunosuppressive proteins in T cells and proteins known to drive drug resistance that together control tumor growth, survival and immune evasion.

Our lead product candidate, tomivosertib, is an oral small-molecule inhibitor of MNK that we are developing in combination with inhibitors of anti-PD-(L)1 therapy, for the treatment of patients with solid tumors. In the second quarter of 2021, we initiated dosing in KICKSTART, our randomized Phase 2b clinical trial evaluating tomivosertib in combination with pembrolizumab in patients with metastatic non-small cell lung cancer ("NSCLC") with PD-L1 expression level greater than or equal to 50% ("PD-L1≥50%"). Pembrolizumab is owned and marketed by Merck for frontline NSCLC and several other indications. We anticipate reporting topline data from the KICKSTART trial in the second half of 2023. Our second product candidate, zotatifin, is a sequence-selective small molecule inhibitor of the RNA helicase eIF4A, a component of the eIF4F complex, and is currently being evaluated in a Phase 1/2 clinical trial in patients with certain solid tumors. We have completed the initial dose escalation portion of this trial and are currently evaluating zotatifin in combination with fulvestrant and abemaciclib ("ZFA triplet") in a Phase 2a open-label expansion cohort in patients with ER+ breast cancer. In light of the favorable safety results observed in the Phase 1/2 clinical trial and target engagement data generated to date, we have also resumed dose escalation of zotatifin in combination with fulvestrant in patients with ER+ breast cancer to determine if a higher dose of zotatifin can be utilized in future clinical studies. To date, we've reported initial data from four cohorts including patients with ER+ breast cancer, which demonstrated that zotatifin appeared to be safe, well tolerated and showed signals of activity, including partial responses in heavily pretreated ER+ breast cancer patients. In addition, in May 2023 we announced positive interim data updates from the Phase 2 ZFA triplet cohort in patients with ER+ metastatic breast cancer ("mBC"). Data from the dose escalation portion of the trial is anticipated in the second half of 2023. We have also completed a Phase 1b clinical trial evaluating zotatifin as an antiviral agent against SARS-CoV-2. The study was a double-blind, randomized, placebo-controlled trial evaluating the safety and antiviral activity of a single dose of zotatifin. In this trial, zotatifin was found to be safe and well-tolerated, and demonstrated favorable trends in several assessments of viral clearance compared to placebo. We have entered into a global collaboration and license agreement with Pfizer for our earliest stage program, inhibitors of eIF4E, and Pfizer is currently conducting investigational new drug application ("IND") enabling studies for this program.

Corporate Information

We were incorporated under the laws of the state of Delaware on October 2, 2020 under the name Locust Walk Acquisition Corp. eFFECTOR Therapeutics, Inc. was incorporated under the laws of the state of Delaware on May 1, 2012. On August 25, 2021, we consummated a merger pursuant to that certain Merger Agreement ("Merger Agreement"), dated as of May 26, 2021, pursuant to which a wholly-owned subsidiary of Locust Walk Acquisition Corp. merged with and into eFFECTOR Therapeutics Operations, Inc. (formerly known as eFFECTOR Therapeutics, Inc.), with eFFECTOR Therapeutics Operations, Inc. becoming our wholly-owned subsidiary. Upon the closing of the merger, we changed our name to eFFECTOR Therapeutics, Inc.

Our corporate headquarters are currently located at 142 North Cedros, Suite B, Solana Beach, California 92075, and our telephone number is (858) 925-8215. Our corporate website address is www.effector.com. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this prospectus or the registration statement of which it forms a part. We have included our website in this prospectus solely as an inactive textual reference.

The Offering			
Common stock offered by us	4,700,000 shares.		
Pre-Funded Warrants offered by us	Pre-Funded Warrants to purchase up to 6,750,382 shares of our common stock at an exercise price of \$0.001 per share. Each Pre-Funded Warrant will be exercisable immediately upon issuance and will not expire until exercised in full. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of such Pre-Funded Warrants. See "Description of Securities Offered—Pre-Funded Warrants" for a discussion on the terms of the Pre-Funded Warrants.		
Concurrent private placement	In a concurrent private placement, we are selling to the investor purchasing the Shares and Pre-Funded Warrants in this offering Purchase Warrants to purchase up to 11,450,382 shares of our common stock at an exercise price of \$0.53 per share. The Purchase Warrants are exercisable immediately following issuance and will have a term of five and one-half years from the initial exercise date. We will receive gross proceeds from exercise of the Purchase Warrants in such concurrent private placement transaction solely to the extent such Purchase Warrants are exercised for cash. The Purchase Warrants and the shares of common stock issuable upon the exercise of the Purchase Warrants are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act.		
Offering price	\$0.655 per share of common stock and \$0.654 per Pre-Funded Warrant.		
Common stock to be outstanding immediately after this offering	53,851,601 shares (assuming exercise in full of all Pre-Funded Warrants for cash and no exercise of the Purchase Warrants).		
Use of proceeds	We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, for general corporate and working capital purposes, including funding our research and development. See "Use of Proceeds."		
Prohibitions on subsequent equity sales	Pursuant to the securities purchase agreement with the investor, we are prohibited from entering into any agreement to issue or announcing the issuance or proposed issuance of any shares of common stock or securities convertible or exercisable into common stock, subject to certain exceptions, for a period commencing on the date of the securities purchase agreement and expiring 30 days from the closing date of the offering.		
	Furthermore, we are prohibited from entering into any agreement to issue common stock or common stock equivalent involving a Variable Rate Transaction (as defined in the securities purchase agreement), subject to certain exceptions, for a period commencing		

	on the date of the securities purchase agreement and expiring one year from the closing date of the offering.
Nasdaq Capital Market listing	Our common stock is listed on the Nasdaq Capital Market under the symbol "EFTR." We do not intend to list the Pre-Funded Warrants on any securities exchange or nationally recognized trading system. Without a trading market, the liquidity of the Pre-Funded Warrants will be extremely limited.
Risk factors	You should read the "Risk Factors" section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our securities.

The number of shares of common stock to be outstanding after this offering is based on 42,401,219 shares outstanding as of March 31, 2023, and excludes as of that date:

- 6,014,990 shares of common stock issuable upon exercise of warrants outstanding as of March 31, 2023, with an exercise price of \$11.50;
- 11,849,297 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2023, at a weighted average exercise price of \$2.13 per share;
- 5,000,000 shares of common stock issuable upon achievement of the Triggering Event as defined in and pursuant to the Merger Agreement;
- 4,292,298 shares of common stock reserved for future issuance under our 2021 Incentive Award Plan and our 2021 Employee Stock Purchase Plan as of March 31, 2023;
- 11,450,382 shares of common stock issuable upon the exercise of the Purchase Warrants offered in the concurrent private placement with an exercise price of \$0.53 per share as described under "Private Placement Transaction"; and
- 801,527 shares of common stock issuable upon exercise of warrants to be issued to the placement agent as compensation in connection with this offering with an exercise price of \$0.8188 per share, as described in "Plan of Distribution."

Unless otherwise indicated, all information contained in this prospectus supplement assumes no exercise of outstanding options or warrants.

Risk Factors

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described below and under the section titled "Risk Factors" in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus supplement and the accompanying prospectus, before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to This Offering

If you purchase shares of our common stock and Pre-Funded Warrants sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The offering price per share of common stock in this offering exceeds the net tangible book value per share of our outstanding common stock. As a result, investors purchasing shares of common stock or Pre-Funded Warrants in this offering may experience immediate and substantial dilution in the net tangible book value of the shares they purchase. For a more detailed discussion of the foregoing, see the section entitled "Dilution" below. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional equity or convertible debt securities, our then existing stockholders may experience dilution and the new securities may have rights senior to those of the securities offered in this offering.

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, for general corporate and working capital purposes, including funding our research and development. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

We do not intend to apply for any listing of the Pre-Funded Warrants on any exchange or nationally recognized trading system, and we do not expect a market to develop for the Pre-Funded Warrants.

We do not intend to apply for any listing of Pre-Funded Warrants on the Nasdaq Capital Market or any other securities exchange or nationally recognized trading system, and we do not expect a market to develop for the Pre-Funded Warrants. Without an active market, the liquidity of the Pre-Funded Warrants will be limited. Further, the existence of the Pre-Funded Warrants and Purchase Warrants may act to reduce both the trading volume and the trading price of our common stock.

The Pre-Funded Warrants purchased in this offering are speculative in nature and do not entitle the holder to any rights as common stockholders until the holder exercises the warrant for shares of our common stock, except as set forth in the Pre-Funded Warrants.

Until you acquire shares of our common stock upon exercise of your Pre-Funded Warrants purchased in this offering, such warrants will not provide you any rights as a common stockholder, such as voting rights, except as

set forth therein. Upon exercise of your Pre-Funded Warrants purchased in this offering, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs on or after the exercise date. Moreover, following this offering, the market value of the Pre-Funded Warrants is uncertain and there can be no assurance that the market value of the Pre-Funded Warrants will equal or exceed their offering price.

Use of Proceeds

We estimate that the net proceeds to us from the sale of common stock and Pre-Funded Warrants in this offering will be approximately \$6.6 million, after deducting placement agent fees and estimated offering expenses payable by us.

We will only receive additional proceeds from the exercise of the Purchase Warrants issuable in connection with the private placement if the Purchase Warrants are exercised and the holders of such Purchase Warrants pay the exercise price in cash upon such exercise and do not utilize the cashless exercise provision of the Purchase Warrants.

We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, for general corporate and working capital purposes, including funding our research and development. The amounts and timing of our actual expenditures will depend on numerous factors, including interactions with and feedback from regulatory authorities, the timing of initiation and progress of our clinical trials and results of such trials, other development efforts for our product candidates, and other factors, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

Description of Securities Offered

Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described in the section entitled "Description of Capital Stock" of the accompanying prospectus and the Description of Registered Securities included as Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the Securities and Exchange Commission on March 8, 2023.

Pre-Funded Warrants

The following summary of certain terms and provisions of the Pre-Funded Warrants that are being offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the Pre-Funded Warrants. Prospective investors should carefully review the terms and provisions of the form of Pre-Funded Warrant for a complete description of the terms and conditions of the Pre-Funded Warrants.

The term "pre-funded" refers to the fact that the purchase price of our common stock in this offering includes almost the entire exercise price that will be paid under the Pre-Funded Warrants, except for a nominal remaining exercise price of \$0.001. The purpose of the Pre-Funded Warrants is to enable investors that may have restrictions on their ability to beneficially own more than 4.99% (or, upon election of the holder, 9.99%) of our outstanding common stock following the consummation of this offering the opportunity to make an investment in the Company without triggering their ownership restrictions, by receiving Pre-Funded Warrants in lieu of our common stock which would result in such ownership of more than 4.99% (or 9.99%), and receive the ability to exercise their option to purchase the shares underlying the Pre-Funded Warrants at such nominal price at a later date.

Duration and Exercise Price. Each Pre-Funded Warrant offered hereby has an initial exercise price per share equal to \$0.001. The Pre-Funded Warrants are immediately exercisable and may be exercised at any time until the Pre-Funded Warrants are exercised in full. The exercise price and number of shares of common stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price.

Exercisability. The Pre-Funded Warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder's warrants to the extent that the holder would own more than 4.99% (or, at the election of the holder, 9.99%) of our outstanding shares of common stock immediately after exercise, except that upon notice from the holder to us, the holder may increase or decrease the amount of ownership of outstanding shares of common stock after exercise, as such percentage ownership is determined in accordance with the terms of the Pre-Funded Warrants, provided that any increase in this limitation shall not be effective until 61 days after notice to us.

Cashless Exercise. In lieu of making the cash payment otherwise contemplated to be made to us upon exercise of a Pre-Funded Warrant in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the Pre-Funded Warrants.

Transferability. Subject to applicable laws, a Pre-Funded Warrant may be transferred at the option of the holder upon surrender of the Pre-Funded Warrant to us together with the appropriate instruments of transfer.

Exchange Listing. There is no trading market available for the Pre-Funded Warrants on any securities exchange or nationally recognized trading system. We do not intend to list the Pre-Funded Warrants on any securities exchange or nationally recognized trading system.

Right as a Stockholder. Except as otherwise provided in the Pre-Funded Warrants or by virtue of such holder's ownership of shares of our common stock, the holders of the Pre-Funded Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their Pre-Funded Warrants.

Fundamental Transaction. In the event of a fundamental transaction, as described in the Pre-Funded Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, or any person or group becoming the beneficial owner of more than 50% of the voting power represented by our outstanding common stock, the holders of the Pre-Funded Warrants will be entitled to receive upon exercise of the Pre-Funded Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such fundamental transaction.

Private Placement Transaction

In a concurrent private placement, we plan to issue and sell to the investor the Purchase Warrants to purchase up to an aggregate of 11,450,382 shares of common stock. The Purchase Warrants have an exercise price equal to \$0.53 per share.

The Purchase Warrants and the shares of common stock issuable upon the exercise of such warrants are not being registered under the Securities Act, are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act. Accordingly, investors may only sell shares of common stock issued upon exercise of the Purchase Warrants pursuant to an effective registration statement under the Securities Act covering the resale of those shares, an exemption under Rule 144 under the Securities Act or another applicable exemption under the Securities Act.

Exercisability. The Purchase Warrants are exercisable immediately following issuance and will have a term of five and one-half years from the initial exercise date. The Purchase Warrants will be exercisable, at the option of the holder, in whole or in part by delivering to us a duly executed exercise notice and, at any time a registration statement registering the issuance of shares of common stock underlying the Purchase Warrants under the Securities Act is effective and available for the issuance of such shares, or an exemption from registration under the Securities Act is available for the issuance of such shares of common stock purchased upon such exercise.

Cashless Exercise. If at the time of exercise there is no effective registration statement registering, or the prospectus contained therein is not available for the issuance of the shares of common stock underlying the Purchase Warrants, then the Purchase Warrants may also be exercised, in whole or in part, at such time by means of a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the warrant.

Exercise Limitation. A holder will not have the right to exercise any portion of the Purchase Warrants if the holder (together with its affiliates) would beneficially own in excess of 4.99% (or, upon election of the holder, 9.99%) of the number of our shares of common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the Purchase Warrants. However, any holder may increase or decrease such percentage, but in no event may such percentage be increased to more than 9.99%, provided that any increase will not be effective until the 61st day after such election.

Exercise Price Adjustment. The exercise price of the Purchase Warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our shares of common stock.

Transferability. Subject to applicable laws, the Purchase Warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing. There is no established trading market for the Purchase Warrants, and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the Purchase Warrants on any national securities exchange or other trading market.

Fundamental Transactions. In the event of any fundamental transaction, as described in the Purchase Warrants and generally including any merger with or into another entity, sale of all or substantially all of our assets, tender offer or exchange offer, or reclassification of our shares of common stock, then upon any subsequent exercise of a Purchase Warrant, the holder will have the right to receive as alternative consideration, for each share of common stock that would have been issuable upon such exercise immediately prior to the occurrence of such fundamental transaction, the number of shares of common stock of the successor or acquiring corporation of our

company, if it is the surviving corporation, and any additional consideration receivable upon or as a result of such transaction by a holder of the number of shares of common stock for which the Purchase Warrant is exercisable immediately prior to such event.

Notwithstanding the foregoing, in the event of a fundamental transaction, we or a successor entity shall, at the holder's option, exercisable at any time concurrently or within thirty (30) days following the consummation of a fundamental transaction, purchase the Purchase Warrant by paying to the holder an amount equal to the Black Scholes Value (as defined in each Purchase Warrant) of the remaining unexercised portion of the Purchase Warrant on the date of the fundamental transaction. If the fundamental transaction is not within our control, the holders of the Purchase Warrants will only be entitled to receive from us or a successor entity the same type or form of consideration (and in the same proportion), at the Black Scholes Value of the unexercised portion of the Purchase Warrant, that is being offered and paid to the holders of our common stock in connection with the fundamental transaction, whether that consideration is in the form of cash, stock or any combination thereof, or whether the holders of our common stock are given the choice to receive alternative forms of consideration in connection with the fundamental transaction.

Rights as a Stockholder. Except as otherwise provided in the Purchase Warrants or by virtue of such holder's ownership of our common stock, the holder of a Purchase Warrant will not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the warrant.

You should review a copy of the securities purchase agreement and a copy of the form of the Purchase Warrant to be issued to the investor under the securities purchase agreement, which are executed or issued in connection with this offering and will be filed as exhibits to a Current Report on Form 8-K that we file with the SEC, for a complete description of the terms and conditions of the Purchase Warrants and the related transaction agreements.

Dilution

If you invest in our securities in this offering, your interest will be diluted to the extent of the difference between the offering price per share and the net tangible book value per share of our common stock after this offering, assuming no value is attributing to the Purchase Warrants issued in the concurrent private placement.

As of March 31, 2023, our net tangible book deficit was \$4.8 million, or \$0.114 per share, based on 42,401,219 shares of our common stock outstanding as of March 31, 2023. Our net tangible book deficit per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of March 31, 2023.

After giving effect to our sale in this offering of 4,700,000 shares of common stock at an offering price of \$0.655 per share and the sale of Pre-Funded Warrants to purchase 6,750,382 shares of common stock at an offering price of \$0.654 per Pre-Funded Warrant and the issuance of the shares of common stock underlying the Pre-Funded Warrants upon the exercise thereof, after deducting placement agent fees and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2023 would have been \$1.8 million, or \$0.034 per share. This represents an immediate increase of net tangible book value of \$0.148 per share to our existing stockholders and an immediate dilution of \$0.621 per share to new investors purchasing securities in this offering. The following table illustrates this per share dilution.

Offering price per share of common stock		\$ 0.655
Net tangible book deficit per share at March 31, 2023	\$0.114	
Increase per share attributable to new investors purchasing shares in this offering		0.148
As adjusted net tangible book value per share as of March 31, 2023, after giving effect to		
this offering		0.034
Dilution per share to new investors purchasing our common stock in this offering		\$ 0.621

The above discussion and table are based on 42,401,219 shares outstanding as of March 31, 2023, and excludes as of that date:

- 6,014,990 shares of common stock issuable upon exercise of warrants outstanding as of March 31, 2023, with an exercise price of \$11.50;
- 11,849,297 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2023, at a weighted average exercise price of \$2.13 per share;
- 5,000,000 shares of common stock issuable upon achievement of the Triggering Event as defined in and pursuant to the Merger Agreement;
- 4,292,298 shares of common stock reserved for future issuance under our 2021 Incentive Award Plan and our 2021 Employee Stock Purchase Plan as of March 31, 2023;
- 11,450,382 shares of common stock issuable upon the exercise of the Purchase Warrants offered in the concurrent private placement with an exercise price of \$0.53 per share as described under "Private Placement Transaction"; and
- 801,527 shares of common stock issuable upon exercise of warrants to be issued to the placement agent as compensation in connection with this offering with an exercise price of \$0.8188 per share, as described in "Plan of Distribution."

To the extent that outstanding options or warrants are exercised, you may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity or convertible debt securities, your ownership will be further diluted.

Plan of Distribution

We engaged H.C. Wainwright & Co., LLC, Wainwright or the placement agent, to act as our exclusive placement agent in connection with this offering. The placement agent is not purchasing or selling any securities offered by us in this offering, nor is it required to arrange for the purchase and sale of any specific number or dollar amount of such securities, other than to use its "reasonable best efforts" to arrange for the sale of such securities by us. Therefore, we may not sell all of securities being offered. The terms of this offering were subject to market conditions and negotiations between us, the placement agent and prospective investors. The placement agent will have no authority to bind us by virtue of the engagement letter. We have entered into a securities purchase agreement directly with an accredited investor who has agreed to purchase securities in this offering. We will only sell securities in this offering to investors who have entered into securities purchase agreements.

Delivery of the securities offered hereby is expected to take place on or about May 31, 2023, subject to satisfaction of certain closing conditions.

We have agreed to pay the placement agent (i) a cash fee equal to 7.0% of the aggregate gross proceeds of this offering, (ii) a management fee equal to 1.0% of the gross proceeds raised in this offering, (iii) a non-accountable expense allowance of \$75,000, and (iv) up to \$15,950 for the clearing expenses of the placement agent in connection with this offering.

We have also agreed to pay Wainwright a tail fee equal to the cash and warrant compensation in this offering if any investor who had been contacted by Wainwright in connection with this offering during the term of our engagement of Wainwright, provides us with capital in any offering during the 12-month period following expiration or termination of our engagement of Wainwright, subject to certain exceptions.

We estimate the total expenses of this offering paid or payable by us will be approximately \$275,000. After deducting the fees due to the placement agent and our estimated expenses in connection with this offering, we expect the net proceeds from this offering will be approximately \$6.6 million.

Subsequent Equity Sales

Under the terms of the securities purchase agreements, from the date of such agreements until 30 days after the closing of this offering, neither we nor any subsidiary shall (i) issue, enter into any agreement to issue or announce the issuance or proposed issuance of any shares of common stock or common stock equivalents, or (ii) file any registration statement or prospectus, or any amendment or supplement thereto, subject to certain exceptions.

We have also agreed under the terms of the securities purchase agreements, until one year after the closing of this offering, not to (i) issue or sell any debt or equity securities that are convertible into, exchangeable or exercisable for, or include the right to receive, additional shares of common stock either (A) at a conversion price, exercise price or exchange rate or other price that is based upon, and/or varies with, the trading prices of or quotations for the shares of common stock at any time after the initial issuance of such debt or equity securities or (B) with a conversion, exercise or exchange price that is subject to being reset at some future date after the initial issuance of such debt or equity security or upon the occurrence of specified or contingent events directly or indirectly related to our business or the market for our common stock or (ii) enter into, or effect a transaction under, any agreement, including, but not limited to, an equity line of credit or an "at-the-market offering", subject to certain exceptions (including our ability to use our "at-the-market" facility with Cantor Fitzgerald & Co. and committed equity with Lincoln Park Capital Fund, LLC following the expiration of a 60-day restrictive period).

Placement Agent Warrants

In addition, we have agreed to issue to the placement agent, or its designees, at the closing of this offering, warrants to purchase 7.0% of the number of shares of our common stock (and shares of common stock underlying the Pre-Funded Warrants) sold in this offering (or warrants to purchase up to 801,527 shares of our common stock). Such warrants will have substantially the same terms as the warrants being sold and issued in the private placement, except that the placement agent's warrants will have a term of exercise equal to five (5) years from the date of the purchase agreement and will have an exercise price equal to 125% of the offering price per share (or \$0.8188 per share). Neither the placement agent's warrants nor the shares of our common stock issuable upon exercise thereof are being registered hereby.

Indemnification

We have agreed to indemnify the placement agent against certain liabilities, including liabilities under the Securities Act and liabilities arising from breaches of representations and warranties contained in our engagement letter with the placement agent. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

Right of First Refusal

We have also granted Wainwright, subject to certain exceptions, a right of first refusal for a period of ten (10) months following the closing of this offering to act as sole book-running manager, sole underwriter or sole placement agent for each and every future debt financing or refinancing and public or private equity offering by us or any of our subsidiaries.

Other Relationships

From time to time, Wainwright may provide in the future various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions. However, except as disclosed in this prospectus supplement, we have no present arrangements with Wainwright for any further services.

Regulation M Compliance

The placement agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the sale of our shares of common stock offered hereby by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. The placement agent will be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of our securities by the placement agent. Under these rules and regulations, the placement agent may not (i) engage in any stabilization activity in connection with our securities; and (ii) bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until they have completed their participation in the distribution.

Trading Market

Our common stock and warrants outstanding prior to this offering are listed on the Nasdaq Capital Market under the symbols "EFTR" and "EFTRW," respectively.

Legal Matters

The validity of the issuance of the securities offered hereby will be passed upon for us by Latham & Watkins LLP, San Diego, California.

Experts

The consolidated financial statements as of December 31, 2022 and 2021 and for the years then ended incorporated by reference in this prospectus supplement and in the registration statement have been so incorporated in reliance on the reports of Ernst & Young LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

Where You Can Find More Information; Information Incorporated By Reference

Available Information

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the accompanying prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is http://www.sec.gov.

Our website address is www.effector.com. The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

Incorporation By Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus supplement, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the

future, that are not deemed "filed" with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 8, 2023;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, filed with the SEC on May 9, 2023;
- the information specifically incorporated by reference into our Annual Report on Form 10-K from our <u>Definitive Proxy Statement on</u> <u>Schedule 14A</u>, filed with the SEC on May 12, 2023; and
- our Current Reports on Form 8-K filed with the SEC on January 5, 2023, February 21, 2023, March 6, 2023, May 19, 2023, and May 25, 2023; and
- the description of our common stock contained in our registration statement on <u>Form 8-A</u>, filed with the SEC on January 7, 2021 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and the accompanying prospectus and deemed to be part of this prospectus supplement and the accompanying prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

eFFECTOR Therapeutics, Inc. Attn: Corporate Secretary 142 North Cedros Avenue, Suite B Solana Beach, California 92075 (858) 925-8215



PROSPECTUS



\$200,000,000 Common Stock

Preferred Stock Debt Securities Warrants Units

We may offer and sell up to \$200.0 million in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement, together with the documents we incorporate by reference, before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and a smaller reporting company as defined under Rule 405 of the Securities Act of 1933, as amended (the "Securities Act"), and, as such, are subject to certain reduced public company reporting requirements.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "<u>RISK FACTORS</u>" ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock and warrants are listed on the Nasdaq Capital Market under the symbols "EFTR" and "EFTRW," respectively. On August 30, 2022, the closing price of our common stock was \$0.60 per share and the closing price of our warrants was \$0.13 per warrant.

As of August 30, 2022, the aggregate market value of our outstanding common stock held by non-affiliates ("public float") was approximately \$47.4 million based on 33,601,705 shares of outstanding common stock as of such date, at a price of \$1.41 per share on July 11, 2022, which was the highest closing sale price of our common stock on the Nasdaq Capital Market within 60 days of the filing date of this registration statement. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the prior 12 calendar month period that ends on and includes the date of this prospectus. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities registered on this registration statement in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is September 9, 2022.

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	1
WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE	2
THE COMPANY	4
<u>RISK FACTORS</u>	5
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	5
USE OF PROCEEDS	6
DIVIDEND POLICY	6
DESCRIPTION OF CAPITAL STOCK	7
DESCRIPTION OF DEBT SECURITIES	14
DESCRIPTION OF WARRANTS	22
DESCRIPTION OF UNITS	24
<u>GLOBAL SECURITIES</u>	25
PLAN OF DISTRIBUTION	29
LEGAL MATTERS	31
EXPERTS	31

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission ("SEC") using a "shelf" registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings, up to a total dollar amount of \$200.0 million as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectus supplement to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectuses), together with the additional information described under the heading "Where You Can Find More Information; Incorporation by Reference."

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of that free writing prospectus. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus supplements or any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus supplements or any applicable free writing prospectus, and under similar headings in othe

When we refer to "eFFECTOR," "we," "our," "us" and the "Company" in this prospectus, we mean eFFECTOR Therapeutics, Inc., unless otherwise specified. When we refer to "you," we mean the potential holders of the applicable series of securities.

We use our trademarks in this prospectus as well as trademarks, trademarks and service marks that are the property of other organizations. Solely for convenience, trademarks and trademarks referred to in this prospectus appear without the (m, m) symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and trademarks.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, including us, who file electronically with the SEC. The address of that website is http://www.sec.gov.

Our website address is www.effector.com. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 16, 2022;
- the information specifically incorporated by reference into our Annual Report on <u>Form 10-K</u> from our Definitive Proxy Statement on <u>Schedule 14A</u>, filed with the SEC on April 20, 2022;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022 and June 30, 2022 filed with the SEC on <u>May 10, 2022</u> and <u>August 9, 2022</u>, respectively;
- our Current Reports on Form 8-K filed with the SEC on January 24, 2022, February 16, 2022, February 24, 2022, March 28, 2022, April 4, 2022, May 26, 2022, June 6, 2022, June 10, 2022 and July 15, 2022; and
- the description of our common stock contained in the registration statement on <u>Form 8-A</u>, filed with the SEC on January 7, 2021, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

eFFECTOR Therapeutics, Inc. Attention: Corporate Secretary 142 North Cedros Avenue, Suite B Solana Beach, California 92075 (858) 925-8215

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

THE COMPANY

We are a clinical-stage biopharmaceutical company pioneering the development of a new class of oncology drugs we refer to as STRIs. Translation is the process in cells whereby the synthesis of proteins is directed by information contained in genetic sequences. We utilized our proprietary selective translation regulation technology platform to internally discover a portfolio of small molecule STRI product candidates. Our product candidates target the eIF4F complex and its activating kinase, mitogen-activated protein kinase interacting kinase ("MNK"). The eIF4F complex is a central node where two of the most frequently mutated signaling pathways in cancer, the PI3K-AKT and RAS-MEK pathways, converge to activate the translation of select mRNA into proteins that are frequent culprits in key disease-driving processes. Inhibition of eIF4F components or MNK simultaneously downregulates multiple disease-driving proteins before they are synthesized. Each of our product candidates is designed to act on a single protein that drives the expression of a network of multiple functionally related proteins, including oncoproteins, immunosuppressive proteins in T cells and proteins known to drive drug resistance that together control tumor growth, survival and immune evasion.

Our lead product candidate, tomivosertib, is an oral small-molecule inhibitor of MNK that we are developing in combination with inhibitors of anti-PD-(L)1 therapy, for the treatment of patients with solid tumors. In June 2021, we initiated dosing in KICKSTART, our randomized Phase 2b clinical trial evaluating tomivosertib in combination with pembrolizumab in patients with metastatic non-small cell lung cancer ("NSCLC"). We updated our trial design to focus on the largest segment of that market, patients who are undergoing their initial, or frontline, course of treatment. The revised trial includes the following two cohorts: (1) "PD-L1 \geq 50% cohort", for patients with PD-(L)1 expression \geq 50% who will receive tomivosertib or placebo in combination with pembrolizumab as their initial therapy; and (2) a new "PD-L1 \geq 1% cohort" for patients with PD-(L)1 expression \geq 1% who will receive tomivosertib or placebo in combination with pembrolizumab as maintenance therapy immediately after completing the platinum-based chemotherapy doublet phase of their frontline treatment without disease progression. We anticipate reporting topline data from both cohorts in the first half of 2023. Our second product candidate, zotatifin, is an inhibitor of eIF4A, a component of the eIF4F complex, and is currently being evaluated in a Phase 1/2 clinical trial in patients with certain solid tumors. We have completed the Phase 1 portion of this trial and are currently enrolling patients in multiple Phase 2a open-label expansion cohorts in biomarker-selected patients with tumors driven by multiple proteins shown in our preclinical studies to be downregulated by zotatifin. In June 2022, we reported positive interim results from the Phase 1/2 dose escalation and expansion trial, with such results showing that zotatifin was generally well tolerated, resulted in suppression of a select set of oncogenic drivers, and demonstrated initial signals of clinical activity in patients with breast cancer. Based on zotatifin's mechanism and results observed to date, we've expanded the cohort evaluating zotatifin in combination with fulvestrant in ER+ breast cancer to 18 patients. In addition, a new cohort evaluating zotatifin in combination with fulvestrant in ER+ breast cancer patients with Cyclin D1 amplification is being planned. We anticipate reporting topline data from current expansion cohorts by the end of 2022, as well as initial overall response data from the Cyclin D1 amplified ER+ breast cancer cohort in the first half of 2023. We are also conducting a Phase 1b clinical trial evaluating zotatifin as an antiviral agent against SARS-CoV-2. We have entered into a global research collaboration and license agreement with Pfizer for our earliest stage program, inhibitors of eIF4E, and Pfizer is currently conducting IND-enabling studies for this program.

We were incorporated as Locust Walk Acquisition Corp. on October 2, 2020. On August 25, 2021 (the "Closing Date"), we consummated the previously announced merger pursuant to that certain Merger Agreement ("Merger Agreement"), dated as of May 26, 2021, by and among us (formerly known as Locust Walk Acquisition Corp.), eFFECTOR Therapeutics Operations, Inc. (formerly known as eFFECTOR Therapeutics, Inc.) ("Old eFFECTOR"), and Locust Walk Merger Sub, Inc. (Merger Sub), pursuant to which Merger Sub merged with and into Old eFFECTOR, with Old eFFECTOR becoming our wholly owned subsidiary (the "Business Combination"). Pursuant to subscription agreements entered into in connection with the Merger Agreement (collectively, the "Subscription Agreements"), certain Selling Securityholders agreed to subscribe for an aggregate of 6,070,003 newly-issued shares of Common Stock at a purchase price of \$10.00 per share for an aggregate purchase price of \$60.7 million (the "PIPE Investment"). On the Closing Date, we consummated the PIPE Investment and we also changed our name to eFFECTOR Therapeutics, Inc. Our principal executive offices are located at 142 North Cedros Avenue, Suite B, Solana Beach, California 92075, and our telephone number is (858) 925-8215.

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained in or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus and the documents incorporated by reference herein, including statements regarding our future results of operations or financial condition, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, the timing and likelihood of regulatory filings and approvals for our product candidates, our ability to commercialize our product candidates, if approved, the impact of COVID-19 and related supply chain disruption on our business, pricing and reimbursement of our product candidates, if approved, the potential to develop future product candidates, the potential benefits of strategic collaborations, the timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a h

In some cases, you can identify forward-looking statements by terms such as "may," "will," "would," "could," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading "Risk Factors" and elsewhere in this prospectus. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to the restrictions contained in any future financing instruments. In addition, our loan and security agreement with Oxford Finance LLC governing our indebtedness contains restrictions on our ability to declare and pay cash dividends on our capital stock.

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DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes some of the terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you and is subject to and qualified in its entirety by reference to our amended and restated certificate of incorporation and amended and restated bylaws, which are filed as exhibits to our most recent Annual Report on Form 10-K and are incorporated by reference herein. We encourage you to read our certificate of incorporation and our bylaws for additional information.

As of June 30, 2022, our authorized capital stock consisted of 1,000,000,000 shares of common stock, \$0.0001 par value per share, and 100,000,000 shares of preferred stock, \$0.0001 par value per share.

Common Stock

Voting Rights

Each holder of our Common Stock is entitled to one vote for each share of our Common Stock held of record by such holder on all matters voted upon by our stockholders, provided, however, that, except as otherwise required in the certificate of incorporation or by applicable law, the holders of our Common Stock will not be entitled to vote on any amendment to our certificate of incorporation that relates solely to the terms of one or more outstanding series of our preferred stock if the holders of such affected series are entitled, either separately or together with the holders of our or more other such series, to vote thereon pursuant to our certificate of incorporation (including any certificate of designation relating to any series of our preferred stock) or pursuant to the DGCL.

Dividend Rights

Subject to any other provisions of the certificate of incorporation, as it may be amended from time to time, holders of shares of our Common Stock are entitled to receive ratably, in proportion to the number of shares of our Common Stock held by them, such dividends and other distributions in cash, stock or property when, as and if declared thereon by our Board from time to time out of assets or funds legally available therefor.

Rights upon Liquidation

Upon our liquidation, dissolution or winding up of our affairs, whether voluntary or involuntary, after payment or provision for payment of our debts and any other payments required by law and amounts payable upon shares of preferred stock ranking senior to the shares of Common Stock upon such dissolution, liquidation or winding up, if any, our remaining net assets will be distributed to the holders of shares of Common Stock upon such dissolution, liquidation or winding up, pro rata on a per share basis.

Other Rights

Holders of our Common Stock do not have preemptive, subscription, redemption or conversion rights. There are no redemption provisions or sinking fund provisions applicable to the Common Stock. All shares of our Common Stock that are outstanding are fully paid and non-assessable. The rights, powers, preferences and privileges of holders of the Common Stock are subject to those of the holders of any shares of our preferred stock that the Board may authorize and issue in the future.

Preferred Stock

Under the terms of the certificate of incorporation, our Board has the authority to issue shares of preferred stock from time to time on terms it may determine, to divide shares of preferred stock into one or more series and to fix the designations, preferences, privileges, and restrictions of preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preference and the number of shares constituting any series



or the designation of any series to the fullest extent permitted by the DGCL. The issuance of our preferred stock could have the effect of decreasing the trading price of our Common Stock, restricting dividends on our capital stock, diluting the voting power of our Common Stock, impairing the liquidation rights of our capital stock, or delaying or preventing a change in control of the company.

The purpose of authorizing our Board to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of the outstanding voting stock. Additionally, the issuance of preferred stock may adversely affect the holders of Common Stock by restricting dividends on the Common Stock, diluting the voting power of the Common Stock or subordinating the liquidation rights of the Common Stock. As a result of these or other factors, the issuance of preferred stock could have an adverse impact on the market price of the Common Stock.

Dividends

Declaration and payment of any dividend is subject to the discretion of our Board. The time and amount of dividends will be dependent upon, among other things, our business prospects, results of operations, financial condition, cash requirements and availability, debt repayment obligations, capital expenditure needs, contractual restrictions, covenants in the agreements governing current and future indebtedness, industry trends, the provisions of Delaware law affecting the payment of dividends and distributions to stockholders and any other factors or considerations our Board may regard as relevant.

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our Board after considering our financial condition, results of operations, capital requirements, business prospects and other factors the Board deems relevant, and subject to the restrictions contained in any future financing instruments. In addition, our loan and security agreement with Oxford Finance LLC governing our indebtedness contains restrictions on our ability to declare and pay cash dividends on our capital stock.

Election of Directors and Vacancies

The number of directors of the Board shall be fixed solely and exclusively by resolution duly adopted from time to time by the Board. The Board is divided into three classes, designated Class I, II and III, with Class I consisting of three directors, Class II consisting of three directors, and Class III consisting of three directors. Each class of directors will be elected by our stockholders every three years.

Under the bylaws, at all meetings of stockholders called for the election of directors, a plurality of the votes properly cast will be sufficient to elect such directors to the Board.

Except as the DGCL may otherwise require and subject to the rights, if any, of the holders of any series of preferred stock, in the interim between annual meetings of stockholders or special meetings of stockholders called for the election of directors and/or the removal of one or more directors and the filling of any vacancy in that connection, newly created directorships and any vacancies on the Board, including unfilled vacancies resulting from the removal of directors, may be filled only by the affirmative vote of a majority of the remaining directors then in office, even though less than a quorum, or by a sole remaining director. All directors will hold office until the expiration of their respective terms of office and until their successors will have been elected and qualified. A director elected or appointed to fill a vacancy resulting from the death, resignation or removal of a director or a newly created directorship will serve for the remainder of the full term of the class of directors in which the new directorship was created or the vacancy occurred and until his or her successor will have been elected and qualified.

Subject to the rights, if any, of any series of our preferred stock, any director may be removed from office only with cause and only by the affirmative vote of the holders of at least two-thirds (66 2/3%) of our outstanding voting stock then entitled to vote at an election of directors. In case the Board or any one or more directors should be so removed, new directors may be elected at the same time for the unexpired portion of the full term of the director or directors so removed.

In addition to the powers and authorities hereinbefore or by statute expressly conferred upon them, the directors are empowered to exercise all such powers and do all such acts and things as may be exercised or done by us, subject, nevertheless, to the provisions of the DGCL, our certificate of incorporation and to any bylaws adopted and in effect from time to time; provided, however, that no bylaw so adopted will invalidate any prior act of the directors which would have been valid if such bylaw had not been adopted.

Notwithstanding the foregoing provisions, any director elected pursuant to the right, if any, of the holders of preferred stock to elect additional directors under specified circumstances will serve for such term or terms and pursuant to such other provisions as specified in the relevant certificate of designations related to the preferred stock.

Quorum

The holders of a majority of the voting power of the capital stock issued and outstanding and entitled to vote thereat, present in person or represented by proxy, will constitute a quorum at all meetings of the stockholders for the transaction of business, except as otherwise required by law or provided by our certificate of incorporation. If, however, such quorum will not be present or represented at any meeting of the stockholders, the holders of a majority of the voting power present in person or represented by proxy, will have power to adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum will be present or represented. At such adjourned meeting at which a quorum will be present or represented, any business may be transacted which might have been transacted at the meeting as originally noticed. If the adjournment is for more than 30 days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting will be given to each stockholder entitled to vote at such adjourned meeting as of the record date fixed for notice of such adjourned meeting.

Registration Rights

In connection with the Closing, we, Old eFFECTOR, the Sponsor and certain stockholders of Old eFFECTOR who received shares of Common Stock pursuant to the Merger Agreement (the "Holders") entered into the Amended and Restated Registration Rights Agreement, pursuant to which we agreed, among other things, to register for resale, pursuant to Rule 415 under the Securities Act, certain shares of our Common Stock and other equity securities that are held by the parties to the agreement. Pursuant to the Registration Rights Agreement, we were obligated to file this registration statement to register the resale of certain of our securities. In addition, subject to certain requirements and customary conditions, including with regard to the number of demand rights that may be exercised, the Holders may demand at any time or from time to time, to sell all or any portion of their registration Rights Agreement also provide the Holders with "piggy-back" registration rights, subject to certain requirements and customary conditions.

We have agreed to pay all expenses in connection with this offering, other than underwriting commissions and discounts, brokerage fees, underwriter marketing costs, and certain legal expenses. The Holders will pay any underwriting commissions and discounts, brokerage fees, underwriter marketing costs, and certain legal expenses relating to the offering. The Amended and Restated Registration Rights Agreement contains customary cross-indemnification provisions, under which we agreed to indemnify Holders in the event of material misstatements or omissions in the registration statement attributable to us, and Holders are obligated to indemnify us for material misstatements or omissions attributable to them.

Pursuant to the Amended and Restated Registration Rights Agreement, the securities will cease to be registrable securities upon the earlier of (i) the date on which such securities have been sold pursuant to an effective registration statement, (ii) the date as of which such securities shall have been otherwise transferred, new certificates for such securities not bearing a legend restricting further transfer shall have been delivered to us and subsequent public distribution of such securities shall not require registration under the Securities Act, (iii) the date as of which such securities have ceased to be outstanding, (iv) the date as of which such registrable securities may be sold without registration pursuant to Rule 144 under the Securities Act (but with no volume, current public information or other requirements, restrictions or limitations) and (v) the date as of which such securities have been sold to, or through, a broker, dealer or underwriter in a public distribution or other public securities transaction.

Pursuant to the Amended and Restated Registration Rights Agreement, which sets forth our registration obligations with respect to the resale of the shares of Common Stock or any other equity securities of the Company (including the Warrants) held by the Selling Securityholders as of the Closing, other than the shares of Common Stock issued in the PIPE Investment, we have agreed to maintain the effectiveness of this registration statement (or an alternative registration statement covering the resale of such shares) until the earlier of (i) such securities have been sold, transferred, disposed of or exchanged pursuant to this registration statement, (ii) all such securities have been transferred and subsequent transfers are not required to be registered under the Securities Act, (iii) such securities are no longer outstanding, (iv) such securities may be sold without registration under Rule 144 without limitations as to the manner of sale or the amount of such securities that may be sold and without the requirement for us to be in compliance with the current public information requirements under Rule 144, or (v) all such securities have been sold to, or through, a broker, dealer or underwriter in a public distribution or other public securities transaction.

We had also agreed to register the resale of shares purchased in the PIPE Investment pursuant to the Subscription Agreements. Pursuant to the Subscription Agreements, which set forth our registration obligations with respect to the resale of the shares of Common Stock issued in the PIPE Investment, we had agreed to use commercially reasonable efforts to maintain the effectiveness of a registration statement until the earlier of (i) the third anniversary of the Closing, (ii) the date on which all such shares of Common Stock have been sold or (iii) the date on which all such shares of Common Stock can be sold under Rule 144 without limitations as to the manner of sale or the amount of such securities that may be sold and without the requirement for us to be in compliance with the current public information requirements under Rule 144.

Pursuant to the Warrants, which sets forth our registration obligations with respect to the issuance of shares of Common Stock upon exercise of the Warrants, we have agreed to use our best efforts to maintain the effectiveness of this registration statement (or an alternative registration statement covering the resale of such shares) until the expiration of the Warrants.

Anti-takeover Effects of Our Certificate of Incorporation and the Bylaws

Our certificate of incorporation and bylaws contain provisions that may delay, defer or discourage another party from acquiring control of us. We expect that these provisions, which are summarized below, will discourage coercive takeover practices or inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with the Board, which we believe may result in an improvement of the terms of any such acquisition in favor of our stockholders. However, they also give the Board the power to discourage acquisitions that some stockholders may favor.

Classified Board of Directors

As indicated above, our certificate of incorporation provides that the Board is divided into three classes of directors, with each class of directors being elected by our stockholders every three years. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of the Board.

Authorized but Unissued Capital Stock

Delaware law does not require stockholder approval for any issuance of authorized shares. However, the listing requirements of Nasdaq, which would apply if and so long as the Common Stock (or Warrants) remains listed on Nasdaq, require stockholder approval of certain issuances equal to or exceeding 20% of the then outstanding voting power or then outstanding number of shares of Common Stock. Additional shares that may be issued in the future may be used for a variety of corporate purposes, including future public offerings, to raise additional capital or to facilitate acquisitions.

One of the effects of the existence of unissued and unreserved Common Stock may be to enable the Board of Directors to issue shares to persons friendly to current management, which issuance could render more difficult or discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise and thereby protect the continuity of management and possibly deprive stockholders of opportunities to sell their shares of Common Stock at prices higher than prevailing market prices.

Special Meeting, Action by Written Consent and Advance Notice Requirements for Stockholder Proposals

Unless otherwise required by law, and subject to the rights, if any, of the holders of any series of preferred stock, special meetings of our stockholders, for any purpose or purposes, may be called only by or at the direction of (i) a majority of the Board, (ii) the chairperson of the Board, (iii) the Chief Executive Officer, or (iv) the President.

Unless otherwise required by law, written notice of a special meeting of stockholders, stating the time, place and purpose or purposes thereof, shall be given to each stockholder entitled to vote at such meeting, not less than 10 or more than 60 days before the date fixed for the meeting. Business transacted at any special meeting of stockholders will be limited to the purposes stated in the notice.

In addition, our bylaws require advance notice procedures for stockholder proposals to be brought before an annual meeting of the stockholders, including the nomination of directors. Stockholders at an annual meeting may only consider the proposals specified in the notice of meeting or brought before the meeting by or at the direction of the Board, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered a timely written notice in proper form to our secretary, of the stockholder's intention to bring such business before the meeting.

These provisions could have the effect of delaying until the next stockholder meeting any stockholder actions, even if such actions are favored by the holders of a majority of our outstanding voting securities.

Amendment to Certificate of Incorporation and Bylaws

The DGCL provides generally that the affirmative vote of a majority of the outstanding stock entitled to vote on amendments to a corporation's certificate of incorporation or bylaws is required to approve such amendment, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage.

Our certificate of incorporation provides that the following provisions therein may be amended, altered, repealed or rescinded only by the affirmative vote of the holders of at least two-thirds (66 2/3%) in voting power of all the then outstanding shares of Common Stock entitled to vote thereon as a class:

- the provisions regarding our preferred stock;
- the provisions regarding the size, classification, appointment, removal and authority of the Board;
- the provisions prohibiting stockholder actions without a meeting;
- the provisions regarding calling special meetings of stockholders;

- the provisions regarding the selection of certain forums for certain specified legal proceedings between our company and our stockholders; and
- the provisions regarding the limited liability of our directors.

Our bylaws may be amended or repealed (A) by the affirmative vote of a majority of the entire Board then in office (subject to any bylaw requiring the affirmative vote of a larger percentage of the members of the Board), or (B) without the approval of the Board, by the affirmative vote of the holders of two-thirds (66 2/3%) of our outstanding voting stock entitled to vote generally in an election of directors, voting together as a single class.

Delaware Anti-Takeover Statute

Section 203 of the DGCL provides that if a person acquires 15% or more of the voting stock of a Delaware corporation, such person becomes an "interested stockholder" and may not engage in certain "business combinations" with the corporation for a period of three years from the time such person acquired 15% or more of the corporation's voting stock, unless:

- 1) the board of directors approves the acquisition of stock or the merger transaction before the time that the person becomes an interested stockholder;
- 2) the interested stockholder owns at least 85% of the outstanding voting stock of the corporation at the time the merger transaction commences (excluding voting stock owned by directors who are also officers and certain employee stock plans); or
- 3) the merger transaction is approved by the board of directors and at a meeting of stockholders, not by written consent, by the affirmative vote of two-thirds (66 2/3%) of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may elect in its certificate of incorporation or bylaws not to be governed by this particular Delaware law.

Generally, a "business combination" includes a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. Subject to certain exceptions, an "interested stockholder" is a person who, together with that person's affiliates and associates, owns, or within the previous three years owned, 15% or more of our voting stock.

Since we have not opted out of Section 203 of the DGCL, it applies to our company. As a result, this provision will make it more difficult for a person who would be an "interested stockholder" to effect various business combinations with us for a three-year period. This provision may encourage companies interested in acquiring our company to negotiate in advance with the Board because the stockholder approval requirement would be avoided if the Board approves either the business combination or the transaction which results in the stockholder becoming an interested stockholder. These provisions also may have the effect of preventing changes in the Board and may make it more difficult to accomplish transactions which stockholders may otherwise deem to be in their best interests.

Limitations on Liability and Indemnification of Officers and Directors

Our certificate of incorporation limits the liability of our directors to the fullest extent permitted by the DGCL, and our bylaws provide that we will indemnify them to the fullest extent permitted by such law. We have entered into agreements to indemnify our directors, executive officers and other employees as determined by our Board. Under the terms of such indemnification agreements, we are required to indemnify each of our directors and officers, to the fullest extent permitted by the laws of the State of Delaware, if the indemnitee acted in good faith and in a manner the indemnitee reasonably believed to be in or not opposed to the best interests of our company. We must indemnify our officers and directors against all reasonable fees, expenses, charges and other costs of any type or nature whatsoever, including any and all expenses and obligations paid or incurred in connection with investigating, defending, being a witness in, participating in (including on appeal), or preparing to defend,

be a witness or participate in any completed, actual, pending or threatened action, suit, claim or proceeding, whether civil, criminal, administrative or investigative, or establishing or enforcing a right to indemnification under the indemnification agreement. The indemnification agreements also require us, if so requested, to advance all reasonable fees, expenses, charges and other costs that such director or officer incurred, provided that such person will return any such advance if it is ultimately determined that such person is not entitled to indemnification by us. Any claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Exclusive Jurisdiction of Certain Actions

Our certificate of incorporation requires, to the fullest extent permitted by law, unless we consent in writing to the selection of an alternative forum, that derivative actions brought on our behalf, actions against any of our directors, officers or stockholders or breach of fiduciary duty, actions asserting a claim arising pursuant to any provision of the DGCL or our certificate of incorporation or bylaws, and actions asserting a claim against us governed by the internal affairs doctrine may be brought only in the Court of Chancery of the State of Delaware and, if brought outside of Delaware, the stockholder bringing the suit will be deemed to have consented to the personal jurisdiction of the state and federal courts in the State of Delaware and service of process on such stockholder's counsel. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, both state and federal courts have jurisdiction to entertain such Securities Act claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, the certificate of incorporation requires that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the sole and exclusive forum for resolving any action asserting a claim arising under the Securities Act and, if brought in a court other than the federal district courts of the United States of America, the stockholder bringing the suit will be deemed to have consented to the personal jurisdiction of the federal district courts of the United States of America and service of process on such stockholder's counsel. However, there is uncertainty as to whether a court would enforce such provision, and investors cannot waive compliance with federal securities laws and the rules and regulations thereunder. Notwithstanding the foregoing, this forum selection provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act, or any other claim for which the federal courts of the United States have exclusive jurisdiction.

Transfer Agent and Registrar

The transfer agent for Common Stock and warrant agent for Public Warrants and Private Placement Warrants is Continental Stock Transfer & Trust Company. The address for Continental Stock Transfer & Trust Company is Attention: Shareholder Relations, 1 State Street, 30th Floor, New York, New York 10004.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee named in the prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, "eFFECTOR," "we," "our" or "us" refer to eFFECTOR Therapeutics, Inc., unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the debt securities of such series may be surrendered for registration of transfer or exchange and where notices and demands to us in respect of the debt securities may be delivered;

- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company ("DTC" or the "Depositary"), or a nominee of the Depositary (we will refer to any debt security represented by a global debt security as a "book-entry debt security"), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a "certificated debt security") as set forth in the applicable prospectus supplement. Except as set forth under the heading "Global Debt Securities and Book-Entry System" below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder. Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depositary, and registered in the name of the Depositary or a nominee of the Depositary. Please see "Global Securities."

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a "successor person") unless:

• we are the surviving corporation or the successor person (if other than eFFECTOR) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;

• immediately after giving effect to the transaction, no Default or Event of Default shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

"Event of Default" means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such
 default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to
 the expiration of the 30-day period);
- default in the payment of principal of any debt security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture or any debt security (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or eFFECTOR and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of eFFECTOR; or
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus

supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture, unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each holder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading "Consolidation, Merger and Sale of Assets";
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;

- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default or event of default in the payment of the principal of, premium or interest on any debt security (except a rescission of
 acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding
 debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading "Consolidation, Merger and Sale of Assets" and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series ("covenant defeasance").

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Securityholders

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the debt securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements is subject to, and qualified in its entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- United States federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled to:

- vote, consent or receive dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of eFFECTOR.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are

exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain U.S. federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of DTC and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depositary to its nominee or by the nominee to the depositary, or by the depositary or its nominee to a successor depositary or to a nominee of the successor depositary.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a "banking organization" within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a "clearing corporation" within the meaning of the New York Uniform Commercial Code; and
- a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants' accounts, thereby eliminating the need for physical movement of securities certificates. "Direct participants" in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation (DTCC). DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC's records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants' records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC's partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC's records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depositary or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility; disbursement of payments to direct participants is the responsibility of DTC; and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depositary with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depositary is not obtained, securities certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depositary for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depositary is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depositary directs. It is expected that these directions will be based upon directions received by the depositary from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as "Clearstream," or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as "Euroclear," either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers' securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositaries, which in turn will hold such interests in customers' securities accounts in such depositaries' names on DTC's books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC's rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositaries; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depositary to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositaries.

Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

Other

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the Nasdaq Capital Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to

dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of eFFECTOR Therapeutics, Inc. Latham & Watkins LLP and certain attorneys in the firm who have rendered, and will continue to render, legal services to us, own shares of our common stock representing in the aggregate less than one percent of the shares of our common stock outstanding. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2021, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.



4,700,000 Shares of Common Stock Pre-Funded Warrants to Purchase up to 6,750,382 Shares of Common Stock Up to 6,750,382 Shares of Common Stock Underlying the Pre-Funded Warrants

PROSPECTUS SUPPLEMENT

H.C. Wainwright & Co.

The date of this prospectus supplement is May 26, 2023